PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference CFO17355WO	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/JP03 /08197	International filing date *(day/month/year)* 27.06.2003	Priority date *(day/month/year)* 28.06.2002

International Patent Classification (IPC) or national classification and IPC

Int.Cl 7

G01N27/64, G01N33/53, G01N37/00, H01J49/00, H01J49/10, H01J49/04

Applicant

CANON KABUSHIKI KAISHA

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 4 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:

   a. ☑ a total of 10 sheets, as follows:

      ☑ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).

      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

   b. ☐ a total of (indicate type and number of electronic carrier(s))_____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

   ☑ Box No. I Basis of the report
   ☐ Box No. II Priority
   ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   ☐ Box No. IV Lack of unity of invention
   ☑ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   ☐ Box No. VI Certain documents cited
   ☐ Box No. VII Certain defects in the international application
   ☐ Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
21.01.2004	04.08.2004
Name and mailing address of the IPEA/JP **Japan Patent Office** 3-4-3, Kasumigaseki, Chiyoda-ku, Tokyo 100-8915, Japan	Authorized officer 2W 2910 Masamitsu TAKABA Telephone No. +81-3-3581-1101 Ext. 3290

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/JP03 /08197

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language _____, which is the language of a translation furnished for the purposes of:

☐ international search (under Rules 12.3 and 23.1(b))
☐ publication of the international application (under Rule 12.4)
☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on (*replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):*

☐ the international application as originally filed/furnished

☑ the description:
pages 1-7,9-10,12-13,15-16,18-21,23-63 as originally filed/furnished
pages* 8,11,14,17,22 received by this Authority on 26.07.2004
pages* _____ received by this Authority on _____

☑ the claims:
pages 64,66-68,71-73,76-77 as originally filed/furnished
pages* _____ as amended (together with any statement) under Article 19
pages* 65,69-70,74-75 received by this Authority on 26.07.2004
pages* _____ received by this Authority on _____

☐ the drawings:
pages _____ as originally filed/furnished
pages* _____ received by this Authority on _____
pages* _____ received by this Authority on _____

☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/figs _____
☐ the sequence listing (specify): _____
☐ any table(s) related to sequence listing (specify): _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/figs _____
☐ the sequence listing (specify): _____
☐ any table(s) related to sequence listing (specify): _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/JP03 / 08197

Box No. V **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	7-12,22-23,31-36	YES
	Claims	1-6,13-21,24-30,37-38	NO
Inventive step (IS)	Claims		YES
	Claims	1-38	NO
Industrial applicability (IA)	Claims	1-38	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

D1: WO 98/20020 A (SEQUENOM, INC.) 1998.05.14
D2: G.Marriott, et al.,"Photomodulation of the nucleating activity of photocleavable cross-linking actin dimer", BIOCHEMISTRY INTERNATIONAL, Vol.26, No.5, 1992, Pages 943-951
D3: "PC BIOTIN AND RELATED PHOTOCLEAVABLE MODIFIERS", Glen Report, Vol.14, No.1, Feb. 2001, Pages 8,9

1. Claims 1-6,13-21,24-30,37-38

The subject matter of claims 1-6,13-21,24-30,37-38 does not appear to be novel nor to involve an inventive step with respect to D1 cited in the ISR. These claims relate to a usage of photocleavable linkers on MALDI-TOF MS. Such usage appears to be known from D1.

(see Page 33 Line 24 - Page 47 Line 14, Page 52 Line 4 - Page 68 Line 9, Page 103 Line 1 - Page 104 Line 11, and Figures 1-7;
- especially:
Page 36 Lines 12-14 : for timing of photocleavage of the linkers, and
Figure 7 : for linking method (1) between a linker having a succinimide ester and a substrate having an amino group, and (2) between the linker and a polymer having a thiol group.)

2. Claims 7-11,22,31-35

The subject matter of claims 7-11,22,31-35 differs from the D1 in the technical feature BNBA-SE as the photocleavable linker. The subject matter of claims 7-11,22,31-35 is therefore novel.

Supplemental Box

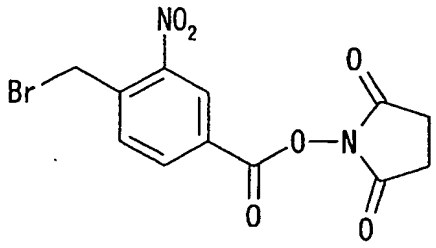
In case the space in any of the preceding boxes is not sufficient.
Continuation of: V. 2

However, D2 discloses the linker and suggests that it is able to be crosslinked to a thiol with an amino group.
Technical features, (1) the linker on Figure 7 in D1 and (2) BNBA-SE in D2 ,have the same function and are related to similar technical fields, especially in the view of photocleavable linker having a site linked to a thiol group and a succinimide ester site.

Therefore, the skilled person in the art would easily conceive the idea of employing the feature BNBA-SE in D2 to substitute the feature the linker on Figure 7 in D1 as a photocleavage linker.

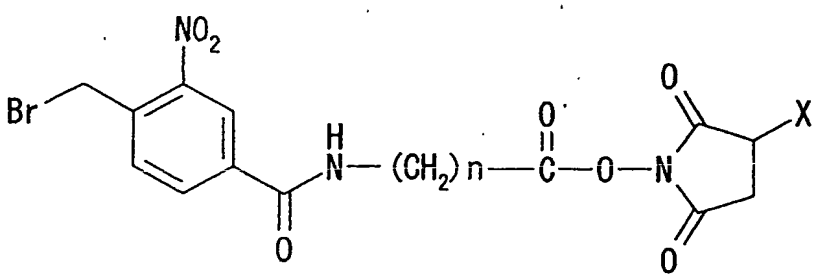
3. Claims 12,23,36

The subject matter of claims 12,23,36 differs from the D1 in the technical feature PC Spacer Phosphoramidite as the photocleavable linker. The subject matter of claims 12,23,36 is therefore novel.
However,both the present invention and that of D3 share the same problem, that is, the usage of an appropriate photocleavable linker, and employ the same technical feature. Therefore, employing the feature PC Spacer Phosphoramidite disclosed in D3 in order to constitute the present invention would have been easily conceived by the person skilled in the art.



Formula I

Also, the structure containing nitrobenzene can be constructed with a compound represented by the following formula II:

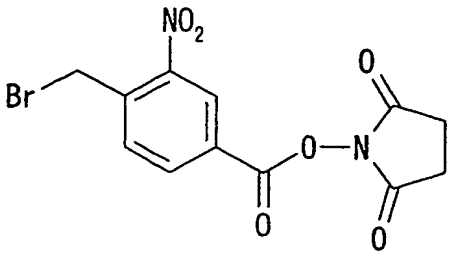


Formula II

(wherein n is 3 to 5, and X is H or SO_3Na).

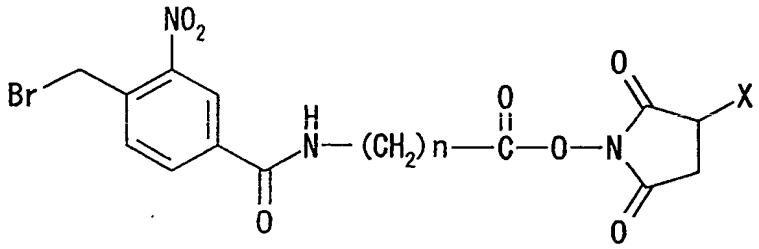
In addition, at that time, it is preferable that the substrate is a glass substrate having a primary amino group formed on the surface, a sulfanil (SH) group is bonded to the terminal of the substance, and the amino group and the sulfanil group are bonded together by a compound represented by the formula I or the formula II through a reaction between the amino group and the succinimide ester site of the compound and a reaction between the sulfanil group and the bromobenzyl site of the compound. Note that,

represented by the following formula I.



Formula I

Also, the structure containing nitrobenzen can be with a compound represented by the following formula II:

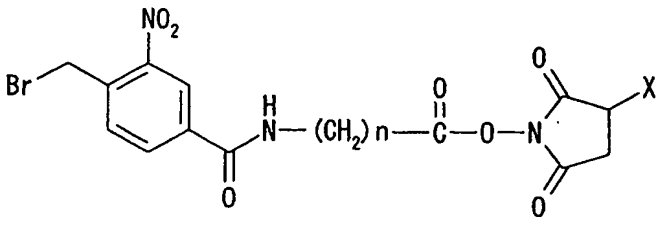


Formula II

(wherein n is 3 to 5, and X is H or SO_3Na).

In addition, at that time, it is preferable that the substrate is a glass substrate having a primary amino group formed on the surface, a sulfanil (SH) group is bonded to the terminal of the substance, and the amino group and the sulfanil group are bonded together by a compound represented by the formula I or the formula II through a reaction between the amino group and the succinimide ester site of the compound and a reaction between the sulfanil group and the bromobenzyl site of the compound. Note that,

be constructed with a compound represented by the following formula II:

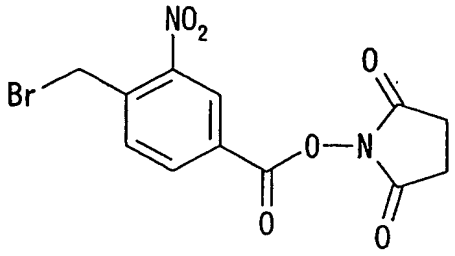


Formula II

(wherein n is 3 to 5, and X is H or SO_3Na).

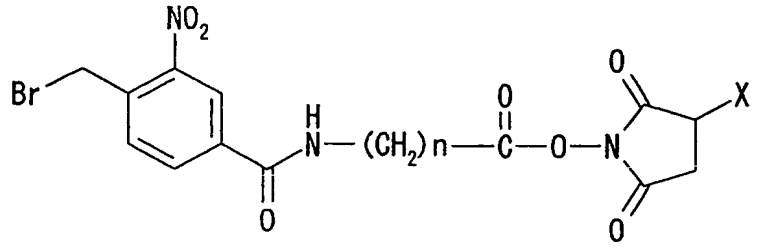
In addition, at that time, it is preferable that the substrate is a glass substrate having a primary amino group formed on the surface, a sulfanil (SH) group is bonded to the terminal of the substance, and the amino group and the sulfanil group are bonded together by a compound represented by the formula I or the formula II through a reaction between the amino group and the succinimide ester site of the compound and a reaction between the sulfanil group and the bromobenzyl site of the compound. Note that, the formation of a primary amino group on the glass substrate is preferably carried out by using a silane coupling agent having the primary amino group.

Alternatively, it is possible that the substrate is a glass substrate having a sulfanil group formed on the surface, an amino group is bonded to the terminal of the substance, and the sulfanil group and the amino group are bonded together by a



Formula I

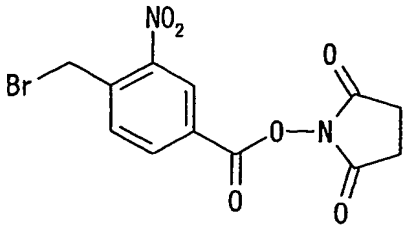
Also, the structure containing nitrobenzene can be constructed with a compound represented by the following formula II:



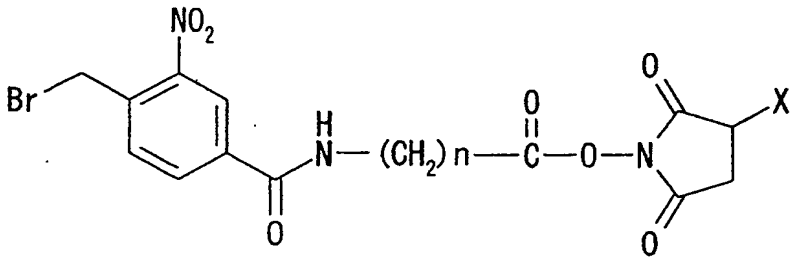
Formula II

(wherein n is 3 to 5, and X is H or SO_3Na).

In addition, at that time, it is preferable that the substrate is a glass substrate having a primary amino group formed on the surface, a sulfanil (SH) group is bonded to the terminal of the substance, and the amino group and the sulfanil group are bonded together by a compound represented by the formula I or the formula II through a reaction between the amino group and the succinimide ester site of the compound and a reaction between the sulfanil group and the bromobenzyl site of the compound. Note that, the formation of a primary amino group on the glass



Formula I



Formula II

(wherein n is 3 to 5, and X is H or SO_3Na).

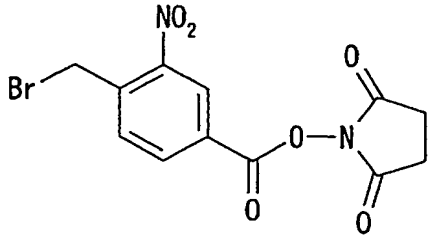
At that time, as the method of fixing a desired substance on a substrate may be used one in which a glass substrate having a primary amino group formed on the surface is used as the substrate, a sulfanil (SH) group is bonded to one end of the substance, and bonding between the amino group and the sulfanil group is carried out by a compound represented by the formula I or formula II, that is, a reaction between the amino group and the succinimido ester site of the compound and a reaction between the sulfanil group and the bromobenzyl site of the compound. In this case, the formation of a primary amino group on the glass substrate can be carried out by using a silane

nitrogen laser beam.

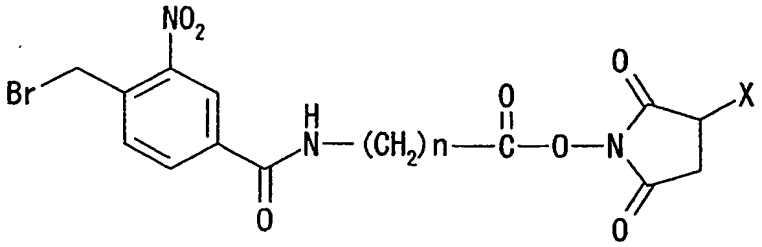
5. The method according to claim 1, wherein the substance fixed on the substrate is nucleic acid.

6. The method according to claim 1, wherein a structure containing nitrobenzene is selected as the partial structure to be disconnected by the irradiation of light.

7. (amended) The method according to claim 6, wherein the structure containing nitrobenzene is constructed with a compound represented by the following formula I or II:



Formula I



Formula II

(wherein n is 3 to 5, and X is H or SO_3Na).

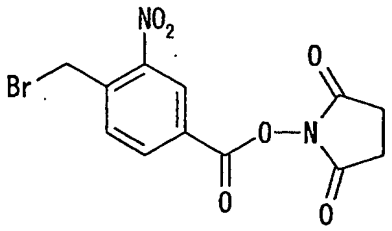
the nucleic acid is DNA.

19. The biochip according to claim 17, wherein the nucleic acid is RNA.

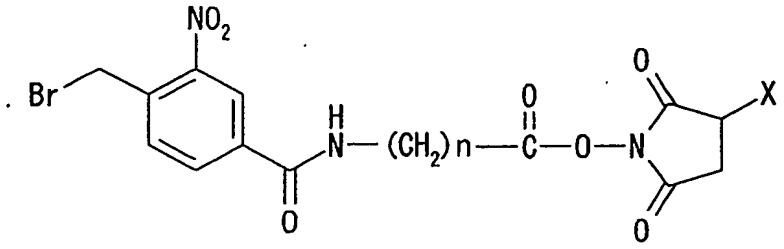
20. The biochip according to claim 17, wherein the nucleic acid is PNA (peptide nucleic acid).

21. The biochip according to claim 16, wherein the partial structure to be disconnected by the irradiation of light has a structure containing nitrobenzene.

22. (amended) The biochip according to claim 21, wherein the structure containing nitrobenzene is constructed with a compound represented by the following formula I or II:



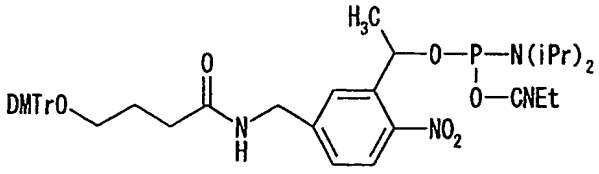
Formula I



Formula II

(wherein n is 3 to 5, and X is H or SO_3Na).

23. The biochip according to claim 21, wherein the structure containing nitrobenzene is constructed with a compound represented by the following formula III:



Formula III

(wherein DMTrO is a dimethoxytrityloxy group and CNEt is a 2-cyanoethyl group).

24. A method of acquiring data on the mass of a bio-related substance on each matrix of a biochip having a plurality of bio-related substances fixed on a substrate in a matrix form and the mass of a substance which interacts with the bio-related substance, the method comprising the steps of:

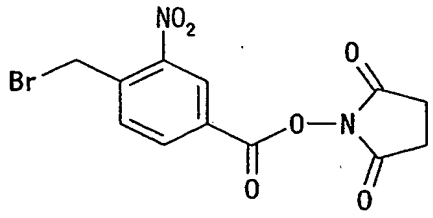
fixing the bio-related substance on each matrix

light used for analysis of the MALDI-TOF MS method.

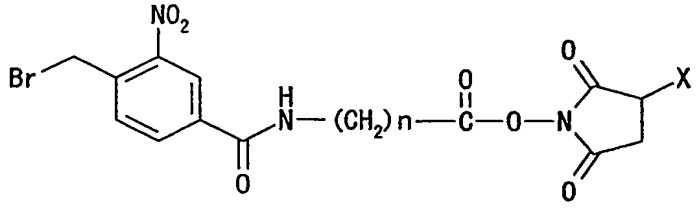
29. The method according to claim 27, wherein the laser light used for analysis of the MALDI-TOF MS method is nitrogen laser light with a wavelength of 337 nm.

30. The method according to claim 27, wherein in the process (5), a structure containing nitrobenzene is selected as the partial structure to be disconnected by the irradiation with light.

31. (amended) The method according to claim 27, wherein the structure containing nitrobenzene is structured using a compound represented by the following formula I or II:



Formula I



Formula II

(where, n is 3 to 5, X=H or SO_3Na).

32. The method according to claim 31, wherein the substrate is a glass substrate on the surface of which a primary amino group is formed, a sulfanil (SH) group is bonded to a 5'-terminal of the primer, and the amino group is bonded to the sulfanil group via a compound represented by the formula I or a compound represented by the formula II by a reaction between the amino group and a succiimidoester site of the compound and a reaction between the sulfanil group and a bromobenzyl site of the compound.

33. The method according to claim 32, wherein the primary amino group is formed on the glass substrate by using a silane coupling agent having a primary amino group.

34. The method according to claim 31, wherein the substrate is a glass substrate on the surface of which a sulfanil group is formed, an amino group is bonded to a 5'-terminal of the primer, and the amino group is bonded to the sulfanil group via a compound represented by the formula I or a compound represented by the formula II by a reaction between the sulfanil group and bromobenzyl site of the compound and a reaction between the amino group and a